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Characteristics of improvements in balance control using vibro-tactile biofeedback of trunk sway for multiple sclerosis patients

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ABSTRACT

Background and aims: Previously, we determined that training with vibrotactile feedback (VTfb) of trunk sway improves MS patients' balance impairment. Here, we posed 5 questions: 1) How many weeks of VTfb training are required to obtain the best short-term carry over effect (CoE) with VTfb? 2) How long does the CoE last once VTfb training terminates? 3) Is the benefit similar for stance and gait? 4) Is position or velocity based VTfb more effective in reducing trunk sway? 5) Do patients' subjective assessments of balance control improve?

Methods: Balance control of 16 MS patients was measured with gyroscopes at the lower trunk. The gyroscopes drove directionally active VTfb in a head-band. Patients trained twice per week with VTfb for 4 weeks to determine when balance control with and without VTfb stopped improving. Thereafter, weekly assessments without VTfb over 4 weeks and at 6 months determined when CoEs ended.

Results: A 20% improvement in balance to normal levels occurred with VTfb. Short term CoEs improved from 15 to 20% ($p \leq 0.001$). Medium term (1–4 weeks) CoEs were constant at 19% ($p \leq 0.001$). At 6 months improvement was not significant, 9%. Most improvement was for lateral sway. Equal improvement occurred when angle position or velocity drove VTfb. Subjectively, balance improvements peaked after 3 weeks of training (32%, $p \leq 0.05$).

Conclusions: 3–4 weeks VTfb training yields clinically relevant sway reductions and subjective improvements for MS patients during stance and gait. The CoEs lasted at least 1 month. Velocity-based VTfb was equally effective as position-based VTfb.

1. Introduction

Multiple sclerosis (MS) is a chronic inflammatory, demyelinating and neurodegenerative disease of the central and peripheral nervous systems [1,2]. In 2013, the number of individuals with MS was estimated to be 2.3 million worldwide [3]. In Switzerland, recent epidemiological estimates indicate that there are approximately 15,000 individuals with MS [4,5].

It is a general finding across several studies that MS patients have impaired balance control [6]. Given the individually highly variable disease-course [7], these balance deficits can arise from combinations of neurological deficits, such as paresis, spasticity, decreased somatosensory proprioception, cerebellar disorders, visual impairment, cognitive impairments and fatigue [8–11].

Cameron & Lord [12] described the most impacting challenges of balance control in patients with MS as (i) a difficulty maintaining the same position without increased sway; (ii) difficulties in moving to the limits of stability; (iii) leaning or moving while standing on one leg, and, (iv) slowed reactions to postural disturbances. These difficulties lead to slower gait speed, presumably as an attempt to reduce roll sway [13], and an increase in falls [12]. As an example of the slowed reactions, Cameron and colleagues [9] investigated the relationship between automatic postural response latencies (reaction times) to support surface perturbations and leg afferent nerve transmission times quantified using somatosensory evoked potential (SSEP) latencies from the stimulation point at the ankle to the recording location at the spinal cord or cerebral

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cortex. It was demonstrated that the automatic postural response latencies were delayed for MS patients and this delay was positively correlated with increased SSEP latencies. Furthermore, ankle torque response amplitudes were increased to compensate for the increased postural response latency. The data of Cameron et al. [9] indicates that one reason pathological responses to balance disturbances occur in individuals with MS is due to a slowed afferent conduction to the central nervous system (CNS) of the proprioceptive signals contributing to balance control. However, reduced efferent input can also result in slowed and weakened reactions to correct individual balance instability [9]. In addition, it is possible that weakened gamma efferent inputs to muscle spindles also effect the sensitivity of afferent fibres to muscle stretch [14].

The findings above suggest that the natural feedforward and feedback balance control systems are altered in MS, leading to slowed proprioceptive-based reaction times and weakened responses. An artificial external feedback system could provide faster perception of movement than compromised natural systems and thereby help improve the balance control of individuals with MS. One possible approach, which was first used for peripheral vestibular loss subjects who had failed to compensate for their reduced balance control, would be to provide vibrotactile feedback (VTfb) of trunk sway [15,16]. The advantage of the VTfb technique is that the threshold of body sway can be set so that an earlier, enhanced conscious perception of movement is signalled by the onset of tactile vibration. The tactile sensations are transmitted to the brain over afferent fibres [17] from locations where the vibrators are placed, such as the waist [18] or head [19], that is, where tactile sensation is often less affected by MS. In bilateral vestibular loss subjects, it has been shown that VTfb reduces sway as a result of these subjects learning to reduce co-activation levels in trunk and leg muscles to levels of healthy controls [20].

Given that improvements in MS patients' reaction times might occur with VTfb in a similar manner to healthy individuals [19], a number of issues need to be considered. These include whether use of VTfb presents a test subject with a dual task, i.e. reducing their ability to concentrate on natural afferent signals and whether position or velocity feedback signals should be used for stance and gait tasks, respectively [21]. From a clinical viewpoint it is important to quantify the duration of the VTfb training that is necessary to obtain a maximal effect on balance control, and the time period over which any subsequent carry-over effect (the effect on balance control after VTfb training ceases) remains present. This information would provide a guideline for determining the time when a patient should return to his/her responsible therapy centre for additional training with VTfb and forms the major focus of this study. Our assumption, based on patient comments, is that patients would prefer this type of rehabilitation based on a carry-over effect in comparison to one where they would need to wear the possibly cosmetically disturbing VTfb equipment continuously.

In randomized cross-over studies, the effect of training sessions with and without VTfb was determined for MS patients [22], as well as for young and elderly heathy individuals [19]. In these studies, the biggest improvements in trunk sway were always demonstrated when participants received the training with feedback and were tested with feedback [19,22].

The aforementioned question of the effect sensory augmentation has on dual tasking (assuming that paying attention to the VTfb represents a dual task) has been investigated for young and elderly healthy adults. Verhoeff et al. [23] found that young adults could reduce sway using VTfb during normal walking, both with and without an additional cognitive or motor dual task. Elderly individuals could likewise reduce sway during walking both with and without an additional motor task but not during an additional cognitive task. We assumed that this result observed with the elderly would be similar, in the worst case, for the middle-aged MS patients aged about 54 years of the current study. For MS patients, other authors, e.g. Prosperini et al. [24], have found that most simultaneously performed dual tasks have little effect on balance control even though stance balance control was worse in MS patients compared to healthy controls. Based on these results we assumed that paying attention to the VTfb during stance and gait trials could not be considered a cognitive dual task limiting balance task abilities and, if it were, there would not be an effect on the improvements in balance control.

The vibrotactile sensory augmentation technique has been investigated for a variety of patient groups, including those with vestibular loss [25]. With the exception of our studies [22], this technique has not yet been applied to patients with MS. Most studies propose that the VTfb device should be worn continuously, thereby not incorporating the possibility of learning and adaptation effects present as carry-over effects in the treatment procedure.

In our recent study, Rust et al. [26] demonstrated that in MS patients two weeks of training with VTfb of trunk sway led in the first week to a rapid improvement in balance control followed by an additional slightly improved balance control in the second week of VTfb training. There was also a carry-over effect present 2 weeks after the training had ended, indicating that both training and carry-over effects might continue to improve further with a longer VTfb training period. Therefore, the aim of the current study was to determine the effect on balance control of four weeks of VTfb training. Our primary interest was to plot the time course of the slower secondary balance control improvement with VTfb training and the time course of reduction of the carry-over effect once VTfb training ceased, given that balance training with VTfb provides a greater improvement in balance control than balance training without VTfb [22]. Information on these time courses would provide relevant clinical information regarding when to retrain patients once the carry-over effect was no longer present. In addition, the training assessment procedure we describe below and in Figure 2 was used in an attempt to answer the question whether the carry-over effect of 8 sessions of training with VTfb is so strong that continuous wear of the VTfb system for improved balance control would not become necessary. Rather, patients would only need to re-train for 1–2 weeks with VTfb once the carry-over effect had worn off. The advantage of the technique used in this study is the simplicity of the feedback, which is directly related to movements of the body's centre of gravity, and the placement of the VTfb at the head. We assumed the VTfb acts as a sensory augmentation of the information received by the proprioceptive and peripheral vestibular systems.

2. Methods

2.1. Participants

The protocol of this interventional study was approved by the local ethics committee (Approval 2014-026 Ethical Committee of North-West and Central Switzerland). All participants provided prior written informed consent to participate in the study. None of the patients had participated in previous studies [22,26] examining the effects of VTfb on

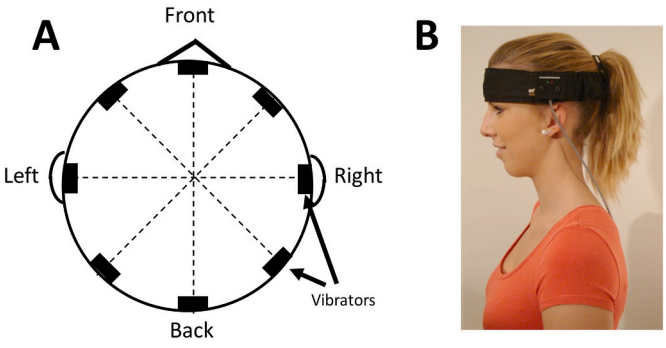

Fig. 1. A Schematic of the spacing of the vibrators in the vibrotactile feedback head-band. B Photograph of the head band as worn by the study subjects.

balance control. All 16 participants were recruited from the neurological outpatient clinic of the University of Basel Hospital, Switzerland. Eleven of the 16 patients were female and 5 patients were male, 13 had relapsing-remitting MS, and 3 suffered from primary-progressive MS. The mean patient age was 54.3 ± 7.1 years, the median Expanded Disability Status Scale (EDSS) score was 3.0 [range 2.5–4.0], and mean disease duration was 12.7 ± 9.1 years. Study inclusion criteria were the diagnosis of MS according to the revised McDonald criteria from 2010 [27], nonexistence of a relapse during the last 6 months before study entry, subjectively reported restrictions to balance, and quantified deficits in balance control as noted during the first assessment (for details, see below). Participants were excluded if they were not able to walk 8 m without walking aids, or had conditions other than MS that might have affected balance (e.g. vestibular impairment, orthopaedic disorders, and severe comorbidities) or had noticeable cognitive or psychiatric disturbances that might have or proved to have affected testing. Table 1 describes the patients' neurological characteristics and disease modifying treatment. The number of patients recruited, 16, was guided by our previous study involving 15 patients for whom a significant effect of VTfb on balance control was noted after 1 week of VTfb training [26] as in the current study.

Participant sensed restrictions in balance control during daily life were estimated using the Dizziness Handicap Inventory (DHI) [28] and the 12-item Multiple Sclerosis Walking Scale (MSWS-12) [29] questionnaires. The DHI consists of 25 questions designed to quantify the subjectively experienced balance deficit. It has demonstrated appropriate reliability and content validity when completed by MS patients [30]. High DHI scores suggest a high subjectively experienced disability. The MSWS-12 is a validated subjective assessment of the walking ability of MS patients [29]. Balance control was measured with a SwayStar™ system (Balance International Innovations GmbH, Switzerland) which contains two fibre-optic gyroscopes mounted on a converted motor cycle kidney belt. These were aligned to measure lower trunk pitch (anterior-posterior sway) and roll (medial-lateral sway) angular velocities. The velocities were sampled at 100 Hz and then transferred to a computer using Bluetooth™ communication. Pitch and roll angles are computed on-line using trapezoid integration of the velocity samples. Prior to participating in the study, subjects underwent a comprehensive clinical neurological examination which included screening for inclusion and exclusion criteria.

2.2. Intervention

Vibrotactile feedback (VTfb) of trunk sway was provided to study participants using an add-on device of Swaystar called Balance Freedom™. This feedback system consists of 8 vibrators positioned at 45-degree intervals around a circular head band providing directionally specific sway information (see Fig. 1). For example, if a sway threshold for forward pitch was exceeded, the vibrator in the middle of the forehead was activated. Likewise, for backward movement exceeding threshold, the vibrator at the back of the head came on. Left and right supra-threshold sway caused the vibrators over the left and right ears, respectively, to be activated. For sway in the diagonal directions, forward and left, for example, the vibrator between the forehead and left ear vibrators was activated when its threshold was exceeded. Thus when the head was aligned in the head straight-ahead position, the vibrotactile feedback (VTfb) provided by the vibrators was aligned with the axes of the gyroscopes. The controller for the vibrators was connected directly with the SwayStar™ unit (see cable in Fig. 1B). Task-specific thresholds for trunk sway angles (used during stance and tandem steps tasks) and angular velocities (used during gait tasks plus an additional tandem steps task) were set in the controller based on pitch and roll measures obtained from the first (baseline) assessment and successively readjusted based on measures from the 3rd, 5th, and 7th assessments (see Fig. 2). The threshold VTfb amplitudes were calculated as 40% of the 90% ranges of pitch and roll sway angle or angular velocity. We used 40% of the 90% ranges based on a previous assessment of the average range of sway reductions achieved by healthy elderly and young normal subjects [19,22]. Thus, the threshold ranges were set at 80% (40% for each side) of the 90% ranges. To determine the 90% ranges, the total peak-to-peak range of each trunk sway variable was determined over the trial duration for a task and this range split into 40 bins. Samples were then sorted into the appropriate bins to build a histogram of the samples. The range from the lower 5% and the upper 95% of the histogram was used to define the 90% range. The thresholds were individually set for each task.

2.3. Procedure

Over a period of 4 weeks, all participants performed a series of assessment and training sequences of gait and stance tasks. The order of assessments and training sessions is presented in Fig. 2. The study

Table 1
Patient neurological characteristics. The following abbreviations have been used: MS, multiple sclerosis; RRMS, relapsing remitting multiple sclerosis; PPMS, primary progressive multiple sclerosis; EDSS, expanded disability status scale; LRE, lower right extremity; LLE, lower left extremity; BLE, both lower extremities; M, motor strength; DHI, Baseline Dizziness Handicap Inventory score; MSWS Baseline MS walking score.

No.	MS type	Disease duration, years	EDSS score	Clinically apparent focal neurological deficits contributing to balance disorder	DHI score	MSWS score	Disease modifying treatment (DMT)
1	RRMS	10	3.0	Slight cerebellar syndrome, motor fatigue	26	22	Natalizumab
2	PPMS	8	3.5	Paraparesis, hip flexion LLE M4/5	40	46	Ocrelizumab
3	PPMS	7	3.0	Slight tetraparesis, mild cerebellar syndrome	54	30	Ocrelizumab
4	PPMS	6	2.5	Slight cerebellar syndrome and motor fatigue	8	20	Ocrelizumab
5	RRMS	34	2.0	Paraparesis, hip flexion both LE M4/5	30	28	Fingolimod
6	RRMS	23	4.0	Paraparesis, hip flexion both LE M4/5, knee flexion both LE M4/5, foot elevation LLE M4/5, slight affection of proprioception BLE	22	24	Leflunomid
7	RRMS	30	4.0	Paraparesis, LLE pronounced, hip and knee flexion LLE M4/5	28	35	Fingolimod
8	RRMS	4	2.5	Slight tetraparesis, motor fatigue	44	24	Fingolimod
9	RRMS	6	3.0	Paraparesis, hip flexion RLE M4/5, discrete residual paresis LLE	28	35	Ocrelizumab
10	RRMS	24	3.5	Spastic paraparesis, hip flexion BLE M4+/5, moderate affection of proprioception BLE	66	38	No DMT
11	RRMS	12	4.0	Spastic paraparesis, hip and knee flexion BLE M4/5, foot elevation RLE M3/5	16	45	Ocrelizumab
12	RRMS	8	3.5	Spastic paraparesis, mainly RLE pronounced, M 4/5	42	43	Ocrelizumab
13	RRMS	16	4.0	Spastic paraparesis, M4/5 BLE, LLE > RLE	54	40	Fingolimod
14	RRMS	23	3.0	Paraparesis RLE > LLE M4+/5	18	16	Ocrelizumab
15	RRMS	13	3.0	Paresis RLE M4+/5	22	24	No DMT
16	RRMS	17	2.5	Slight cerebellar syndrome, motor fatigue, moderate affection of proprioception BLE	8	15	Tecfidera

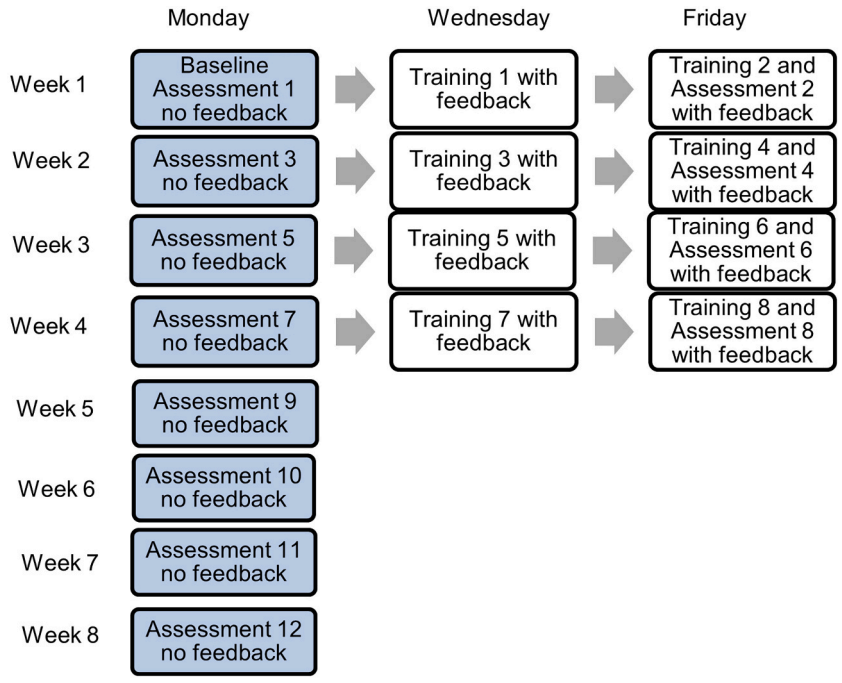

Fig. 2. Schema of the timing of balance assessments and training sessions, with and without, vibrotactile balance feedback of trunk sway. The subjects were seen 3 times a week over 4 weeks for assessments [1–8] and training, then once a week for assessments only [9–12] for a further over 4 weeks. A final assessment [13] took place 6 months later.

procedure consisted of 2 phases: first, an intervention (i.e. training) phase during weeks 1 to 4 when training with VTfb of trunk sway was provided and; second, a phase, monitoring the decrease in the carry-over effect every week for 4 weeks and at 6 months after VTfb training had ceased. For 4 subjects we also monitored the carry-over effect at 2 and 4 months after training ceased. The assessments during the carry-over monitoring phase were all performed without VTfb. During the training phase, assessments without VTfb were always carried out on Mondays. The assessments without VTfb were used to set (week 1) and reset (weeks 2–4) the VTfb thresholds for the training with VTfb. The VTfb device was not worn as a placebo during these assessments. In weeks 2–4, the assessment on Monday was also used to assess the short term (3 days) carry-over effect of VTfb training. Training with VTfb was performed on Wednesdays and Fridays during weeks 1 to 4. During training each task was performed 5 times. The training with VTfb occurred before the assessments with VTfb on Fridays of weeks 1 to 4 (see Fig. 2). For weeks 1 to 4 the assessments on Fridays with VTfb provided information on whether on-line VTfb after training with VTfb aided balance control more than the carry-over effect. Training sessions lasted approximately 30 min and assessment sessions 15 min. A break of 5 min was provided between training and assessment on Fridays to avoid fatigue. Assessments 1, 3, 5 and 7 in weeks 1 to 4, respectively, were performed with no VTfb and assessments 2, 4, 6 and 8 in the same weeks with VTfb. All of the following assessments [9 to 12] were without VTfb (see Fig. 2). We estimated the time course of the medium-term carry-over effect from the assessments 9 to 12 using simple regression analysis. The estimated values of projected balance control at 6 months post training were different from the actual assessment values at 6 months. However, the values of our primary balance measure (BCI- for definition see below) at 6 months were also not significantly different from baseline measures (Fig. 3C). Therefore, we introduced additional examinations at 2 and 4 months for the last 4 patients we tested in order to obtain a preliminary estimate of the earliest time-point when the carry-over effect was no longer present.

2.4. Rationale for total duration of VTfb training and assessment sessions

The current study was designed to determine the characteristics of improvements in balance control during VTfb training and subsequent carry-over effects once training sessions were terminated. In a previous study [22] we investigated the greater improvement in balance control with VTfb compared with training alone (without VTfb) for MS patients in a randomized cross-over study. Therefore, no comparison was made of the effect of training without VTfb in this study. In another prior study, Rust et al. [26] noted that the training and carry-over observation periods were too short, with 2 weeks, to describe the time-course characteristics of short-term carry-over effects after the initial improvement in the first week of training. Therefore, for the current study, the total duration of VTfb training and assessments sessions was extended to 4 weeks with 4 weeks of weekly follow-up. We expected a similar initial improvement in balance control with VTfb as in the previous studies [22,26] followed by a marked continuous improvement over the 4 weeks of training accompanied by an improvement in the subjectively experienced balance deficit as noted in the DHI questionnaires. In contrast, we expected the medium-term carry-over effect on balance control and DHI values to worsen during the 4 weeks post training at the same rate as the preceding short-term improvement.

2.5. Assessment and training tasks

The same 11 tasks were used for the assessments and training sessions (Table 2). Selection of tasks was based on protocols developed by Tinetti [31] and Shumway-Cook and Horak [32] as well as our previous studies, which indicated the ability of these tasks to determine the presence of subclinical balance disorders in MS patients [33,34]. Assessments and training were always performed without shoes to avoid measurement variations due to shoe types. To avoid diurnal differences in fatigue levels affecting the results, assessments and training were always performed at the same preferred time of the day for each patient.

For two-legged stance tasks, participants were asked to stand still with eyes open or closed on a firm or foam surface in a normal, comfortable standing position, lateral borders of the feet hip width

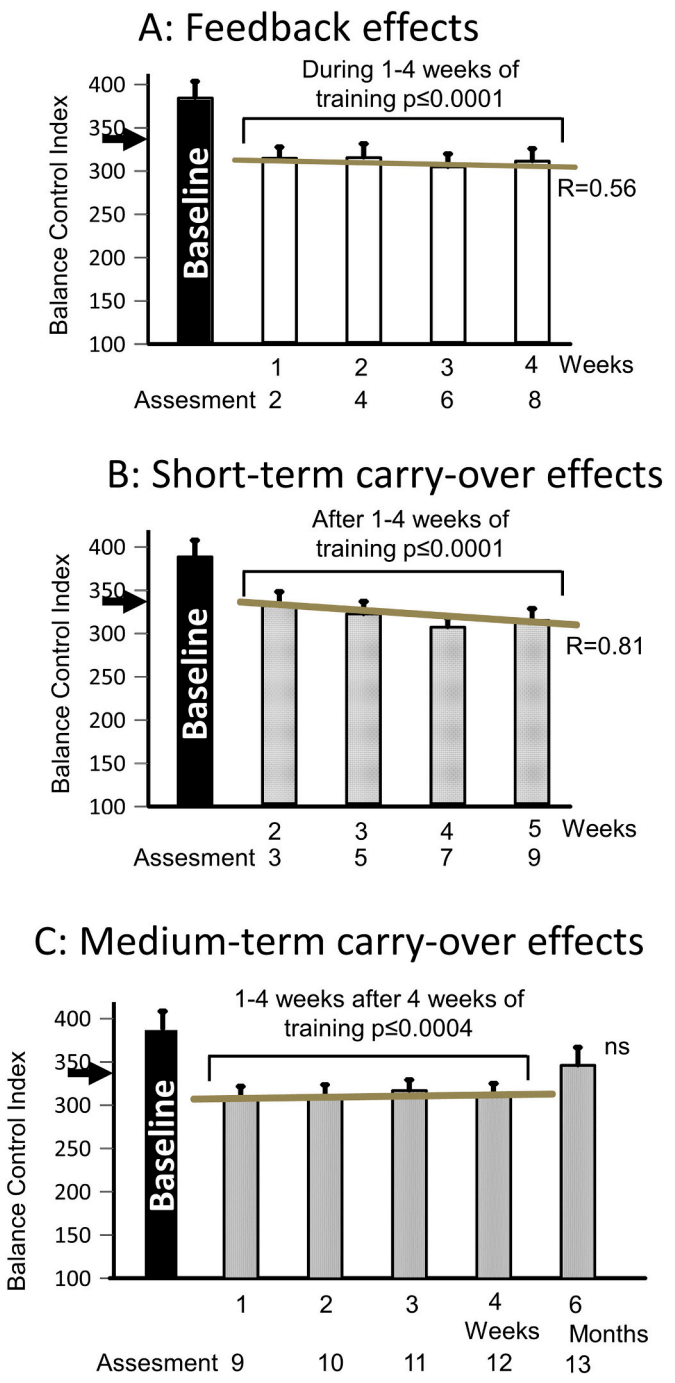

Fig. 3. Mean balance control Index (BCI) values for the first assessment, labelled "baseline", in comparison to subsequent assessments. A: for the assessments with on-line feedback – labelled "feedback effect", B: for the short term carry-over effect during training (assessments with no feedback present), and C: for the medium term carry-over effect after VTfb training ceased. The height of the column represents the mean population sample value for each assessment and the vertical bar on the column, the standard error of the mean. The upper 95% limit of BCI values for healthy control subjects of the same mean age (±5 years) as the study MS patients is shown by the horizontal arrows on the ordinates (data from Hegeman et al. [36]). The post-hoc *p*-values for the multilevel model comparison between assessment 1 and the assessment number noted below the column is listed above the columns. The *p* values for fixed effects are still significant ($p \leq 0.0125$) in panels A, B and C after Bonferroni corrections for 4 comparisons (that is, for example, assessment 1 with 2, 4, 6, and 8). A linear regression line has been drawn through the BCI means over 4 weeks and its coefficient (R) listed to the right the columns, except in C for which R was not significant.

Table 2
Order of stance and gait tasks for assessment and during training sessions.

Task (and task abbreviations)
1. Standing on 2 legs, eyes closed, 20 s (s2ec).
2. Standing on 1 leg, eyes open, 20 s (s1eo).
3. Standing on 2 legs, eyes open, on foam, 20 s (s2eof).
4. Standing on 2 legs, eyes closed, on foam, 20 s (s2ecf).
5. Tandem stance, eyes open, 30 s (tanS)
6. 8 tandem steps, eyes open (position feedback) (tan8_pos).
7. Walking 3 m while pitching the head up and down (w3hp).
8. Walking 3 m, eyes closed (w3ec).
9. Walking over 4 low barriers (barriers)
10. Walking 8 m, eyes open (w8meo).
11. 8 tandem steps, eyes open (velocity feedback) (tan8_vel).

apart, and arms hanging alongside the trunk. The foam surface was 10 cm high, 44 cm width and 204 cm long and had a density of 25 kg/m^3. For eyes open stance tasks, patients were asked to focus on a point at eye height 5 m away. During one-legged tasks, patients chose their better leg to stand on. Stabilizing their raised leg against the standing leg was not allowed. All walking tasks (with eyes closed, with head pitching up and down, or walking over 4 low barriers) were measured over 3 m, except walking 8 m with eyes open. The barriers were 24 cm in height and spaced one meter apart. During all tasks patients were asked not to talk and a spotter stood next to them to aid in case of a loss of balance control. For the assessment sequences, each task was performed once and in training sequences, each task was repeated five times. Only 1 trial of each task was performed during the assessments as we wanted to avoid tiring the MS patients which we presumed would lead to greater balance variability [35]. Theoretically, it would have been possible to use the VTfb training trials for the assessments with VTfb. However, we decided to keep the assessment comparisons as similar as possible. Tasks were stopped if the patient lost balance, for example, needing to take a step during 2-legged stance trials,or if the non-stance foot touched the floor during 1-legged stance trials, or when the task was completed. Only data prior to the loss of balance was analysed. During the training and the assessment sequences, patients were requested to sway as little as possible. When the patients received VTfb of trunk sway, they were requested to try to avoid activating the vibrotactile transducers or to move away from the direction indicated by feedback if the VTfb was activated.

2.6. Outcome measures

For each task of the assessments, peak-to-peak and 90% ranges for pitch velocity (pv), pitch angle (pa), roll velocity (rv) and roll angle (ra) and duration (dur) were measured. Shortened durations, due to lost control of balance during a gait task, were not entered into the analysis in order to avoid such durations representing a fast task completion. We concentrated on one primary measure, a global balance control index (BCI) to compare balance control between assessments. The BCI is a single value which represents a summary of the results from several tasks. That is, the index combines peak-to-peak measures from several different tasks into one value. Thus, the BCI is an additive composite score based on measures from several tasks: From the task standing on two legs on foam with eyes closed (s2ecf) (2 * pv), for walking 8 tandem steps (tan8_pos) (1 * ra), for walking 3 m eyes closed (w3ec) (1.5 * pv + 20 * duration (dur)), for walking 3 m while pitching the head up and down (w3hp) (1.5 * pv). Task abbreviations are also listed in Table 2. That is

$$BCI = 2*s2ecf_{pv} + tan8_{ra} + 1.5*w3ec_{pv} + 20*w3ec_{dur} + 1.5*w3hp_{pv}$$

[36].

The basis for this selection of measures and coefficients in the BCI is a step-wise discriminant analysis described in Allum and Adkin [37] and Hegeman et al. [36] as a way to identify balance control deficits in

peripheral vestibular loss patients in comparison to healthy controls. This combination of the selected balance outcome measures has also been shown to have a high accuracy in detecting MS patients with impaired balance control [34]. When this index revealed differences, 90% ranges of all trunk sway measures and task durations were examined as secondary measures.

Subjective balance impairment was assessed using the above mentioned DHI and MSWS-12 patient-reported outcome measures (PROMs) at beginning of each week when patients were seen weekly (weeks 1 to 8) and then just before the assessment at 6 months, in order to capture subjective carry-over effects.

2.7. Statistical analysis

We applied multilevel linear models to the data using the maximum likelihood method. Within the model, participant scores were defined to be dependent on the different assessment time points [38]. In order to allow effects to vary across entities, "participants" were set as random effects [38].

Posthoc data from assessment 1 was compared with the data for the subsequent assessments provided the factor "assessment time" was significant ($p \leq 0.05$). Data from the following groups of assessments was compared to the baseline assessment 1 to provide confirmation of the following hypotheses using:

- Assessments 2, 4, 6, and 8 – to evaluate the assumed increasingly positive effect with time of on-line VTfb on balance control during the 4 week training period. Fig. 2 describes the organisation of the assessments.
- Assessments 3, 5, 7 and 9 – to evaluate the assumed increasing positive effect with time of the short-term carry -over effect of VTfb training on balance control and PROMs during the 4 week training period.
- Assessments 9, 10, 11, 12 – to evaluate the assumed decreasing medium-term carry-over effect of VTfb training on balance control and PROMs in the 4 weeks after VTfb training had ceased. Note that assessment 9 occurred 3 days after the last training and online VTfb assessment session and was also the first of the 4 weeks of assessments post VTfb training.
- Assessment 13 - to evaluate the assumed terminated long-term carry-over effect of VTfb training on balance control and PROMs 6 months after VTfb training had ceased.

BCI values, mean trial duration, the mean of the 90% ranges for pv, pa, rv, and ra, and the mean PROM values were compared between assessments within the multilevel linear fixed effects model. Separately, comparisons between the balance measurements and PROM values of assessment 1 with those of assessment 13 (at 6 months post training) were performed with the Wilcoxon signed rank *t*-test. Because of the large time span (5 months) between assessments 12 and 13 we required that both within the multilevel model and the Wilcoxon signed rank t-test be significant when comparing assessment 13 with baseline (Assessment 1). The level of alpha was set at 5% for the fixed effects model. The subsequent post-hoc analyses were corrected for multiple comparisons using a Bonferroni correction.

All analyses were performed in RStudio, Version 1.3.1073 [39]. For the multilevel models, the R-package "nlme", Version 3.1-148 was used [40].

Table 3
Statistical descriptives for Balance Control Index (BCI) values at baseline (assessment 1), during the 4 weeks of training (assessments 2 to 9, and 1 to 4 weeks and 6 months after training ceased (assessments 9 to 13). The following abbreviations have been used: N stands for number of cases; sem for standard error of the mean; sd for standard deviation.

N = 16 (except Ass 8 = 15)	Baseline	Feedback effects			
BCI		After 1 week of training	After 2 weeks of training	After 3 weeks of training	After 4 weeks of training
	Assessment 1	Assessment 2	Assessment 4	Assessment 6	Assessment 8
Mean	384	315	315	304	311
Median	363	301	310	293	291
sem	19.4	13.0	15.1	13.9	15.4
sd	77.8	51.9	60.5	55.8	59.5
Max-Min	545–284	417–252	452–226	424–220	450–236
N = 16		Short-term carry-over effects			
BCI	Baseline Assessment 1	After 1 week of training Assessment 3	After 2 weeks of training Assessment 5	After 3 weeks of training Assessment 7	After 4 weeks of training Assessment 9
Mean	384	328	319	303	311
median	363	325	323	293	304
sem	19.4	16.2	14.6	11.0	12.5
sd	77.8	64.7	58.5	44.0	50.1
Max-Min	545–284	443–243	415–197	394–239	424–228

N = 16 (except 11 & 12 = 15)		Medium and long-term carry-over effects				
BCI	Baseline	1 week after training ceased	2 weeks after training ceased	3 weeks after training ceased	4 weeks after training ceased	6 months after training ceased
	Assessment 1	Assessment 9	Assessment 10	Assessment 11	Assessment 12	Assessment 13
Mean	384	311	323	319	314	346
median	363	304	289	299	336	335
sem	19.4	12.5	17.2	12.5	13.5	19.7
sd	77.8	50.1	66.4	48.5	52.3	79.0
Max-Min	545–284	424–228	480–233	412–250	378–227	547–233

3. Results

3.1. Improvements in balance scores

Fig. 3A, B and C illustrate the effects of VTfb on the global balance control index (BCI) described in the methods section. Table 3 lists the statistical descriptives of the BCI values. The assessments when VTfb was present (Fig. 3A and Table 3) were associated with a significant reduction (improvement) in the BCI ($p \leq 0.0001$) over the first 4 weeks of training compared to baseline measures. Almost all of the reduction (18%) occurred in the first week (Fig. 3A: BCI mean baseline value equal to 384.4 ± 19.4 sem compared to 314.5 ± 13.0 for assessment 2) as indicated by changes in intercept values of our statistical model (−70 to −76). Independently, the regression line in Fig. 3A (BCI = −2.12× +317, where x is weeks) also shows that there was a gradual reduction in mean BCI values over training weeks 2 through 4.

Short-term carry-over effects, measured 3 days after a previous training with VTfb on Fridays (Fig. 3B and Table 3), were observed when balance control was tested without VTfb during the first 4 weeks. For these assessments, BCI values were in the first and second training week slightly larger (less reduced) than when tested with VTfb but decreased (improved) more rapidly (model intercept values changed from −56 to-75, see also regression line (BCI = −6.62× +332) in Fig. 3B) so that at 4 weeks there was no difference between feedback and short-term carry-over effects (both 19% improvements). Concerning the medium term carry-over effects over the 4 weeks post VTfb training, the BCI values remained constant (no significant regression) with a value of ca. 312 (19% improvement – see Fig. 3C). However, at 6 months post training the BCI value was not significantly less than baseline (345.9 ± 19.7 (sem) see also Fig. 3C and Table 4). Our observations with a limited number of patients indicated that at 2 months the BCI was still significantly lower baseline (296.1 ± 27.9, $p = 0.05$) but not at 4 months (337.6 ± 32.4 $p > 0.05$).

Table 4 provides an overview of the significant improvements for each task variable when considering the feedback and carry-over effects. It can be noted by the density of the symbols that the feedback effect was stronger than for the medium term carry-over effects (trend $p = 0.1$ seen in a pair-wise proportionality test). The variables in order of roll angle, roll velocity and pitch angle were most often significant across feedback effects and less significant for medium-term carry-over effects, except for task duration which was most significant for the medium term carry-over effect (see totals of Table 4 in row labelled "total of 11"). The tasks in Table 4 are arranged in order of the number of significant variables per task (see totals in Table 4 in column labelled "total of 15"). Standing on one leg and other gait tasks, emphasising periods of one-legged stance (walking tandem steps and walking over low barriers), show the highest number of significant variables, standing on 2 legs with eyes closed and walking 8 m with eyes open, the least. Table 4 also indicates which tasks contributed most to the improvement in the BCI, namely: tandem steps, walking 3 m with head pitching and standing on 2 legs, eyes closed on foam.

3.2. Differences between angle and angular velocity feedback

We examined the influence of angle and angular velocity based VTfb on tandem gait expecting to find that angle feedback improved roll angle more, and angular velocity feedback roll angular velocity more. As Figs. 4 and 5 illustrate there was no difference between the two types of feedback for the feedback and carry-over effects. Both improved roll angles and roll velocity equally with the greatest improvement occurring when VTfb was present (on-line) rather than as a carry-over effect (Figs. 4 and 5).

3.3. Patients' subjective assessments of balance capabilities

The MSWS-12 and DHI questionnaires were used to assess patients' subjectively perceived balance capabilities. The analysis of data from both PROMs showed a significant improvement (lower scores), both during and after VTfb training (see Figs. 6 and 7, Table 5). The effect of VTfb training on the MSWS-12 scores was constantly small (ca. 9%) but statistically significant with respect to baseline (assessment 1).

Interestingly, the effect of VTfb on reducing DHI scores was initially similarly low (11.5%). This effect improved showing decreased DHI values progressively over the 4 weeks of training (model intercept values and linear regression of mean values, (DHI = −2.46× +30.1, where x equals weeks, $R = 0.92$, $p = 0.05$) to reach an improvement of 32% at 4 weeks as noted at assessment 9 (see Fig. 7A, B and Table 5). These scores were not, however, significantly correlated with sway measures. For

Table 4
Overview of trunk sway variables (90% ranges) and trial durations which had 2 or more Wilcoxon t-test values with a significance $p < 0.05$ for each of 5 assessment comparisons (roll and pitch angle, roll and pitch velocity, duration) with baseline assessment 1. That is, for example, roll angle, for assessment 1 was compared with roll angle for feedback effect assessments 2, 4, 6, 8, short term carry-over effect assessments 3, 5, 7, 9, and medium term carry-over effect assessments 9, 10, 11, 12. Sway angle, sway angular velocity and duration variables fulfilling this criterion are marked ▲. Thus for roll angle feedback assessments, 2 of the comparisons of 1vs2, 1vs4, 1vs6 and 1vs8 would need to be significant in order to be marked in the table with ▲. The tasks are arranged in order the number of times this criterion is fulfilled across assessments (see end column labelled "Total of 15"). The number of times the same criterion was fulfilled per variable and comparison set is listed in the lowest row labelled "Total of 11". The following abbreviations have been used: vel, velocity; Dur, Duration; eo, eyes open; ec, eyes closed; s1, stance on 1 leg; s2, stance on 2 legs; tan8, 8 tandem steps; _vel, with angular velocity feedback; _pos, with angle position feedback; wob, walking over low barriers; w3, walk 3 m; w8, walk 8 m; hp., head pitching up and down; tanS, tandem stance; f, foam surface. Comparisons of duration were not made for the following stance trials because of ceiling effects in the data tanS, s2ecf, s2ec and s2eof.

Task	Feedback effect (assessments 2, 4, 6, 8)					Short term carry-over effect (assessments 3, 5, 7, 9)					Medium term carry-over effect (assessments 9,10,11,12)					Total of 15
	Roll angle	Pitch angle	Roll vel.	Pitch vel.	Dur.	Roll angle	Pitch angle	Roll vel.	Pitch vel.	Dur.	Roll angle	Pitch angle	Roll vel.	Pitch vel.	Dur.	
tan8_vel	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	15
s1eo	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲	▲			▲	▲	13
tan8_pos	▲	▲	▲	▲	▲	▲	▲			▲	▲	▲			▲	11
tanS	▲	▲	▲	▲		▲	▲	▲	▲					▲		9
wob	▲	▲	▲	▲		▲				▲	▲		▲		▲	9
w3hp	▲	▲	▲			▲	▲			▲	▲				▲	8
s2ecf	▲	▲	▲			▲	▲	▲					▲	▲		8
w3ec	▲		▲		▲	▲				▲	▲				▲	7
s2ec	▲					▲		▲	▲				▲	▲		6
w8eo	▲		▲		▲										▲	4
s2eof	▲	▲									▲		▲			4
Total of 11	11	8	9	5	5	9	6	5	4	6	7	2	5	5	7	

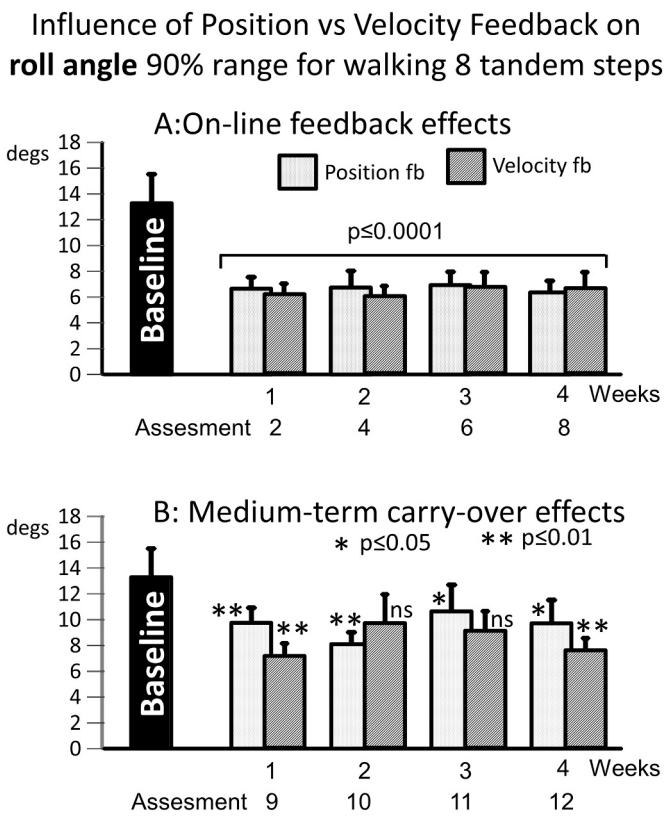

Fig. 4. Mean population sample values of the 90% range of trunk roll sway angle for the task of walking 8 tandem steps with either angle or angular velocity feedback. The height of the columns represents the mean population values and the vertical bars on the columns the standard error of the mean. The value for the first, baseline, assessment is shown as a filled column on the left. A: On-line feedback effects for assessments 2, 4, 6, and 8 for which either position or velocity feedback was provided. B Medium-term carry-over effects observed in assessments 9, 10, 11 and 12 in the 4 weeks subsequent to feedback training. The p-value, prior to a Bonferroni correction of the mean value for each assessment with respect to baseline, is noted on the columns. For the p-value to remain significant after the Bonferroni correction, p must be ≤0.01 prior to correction. ns stands for not significant.

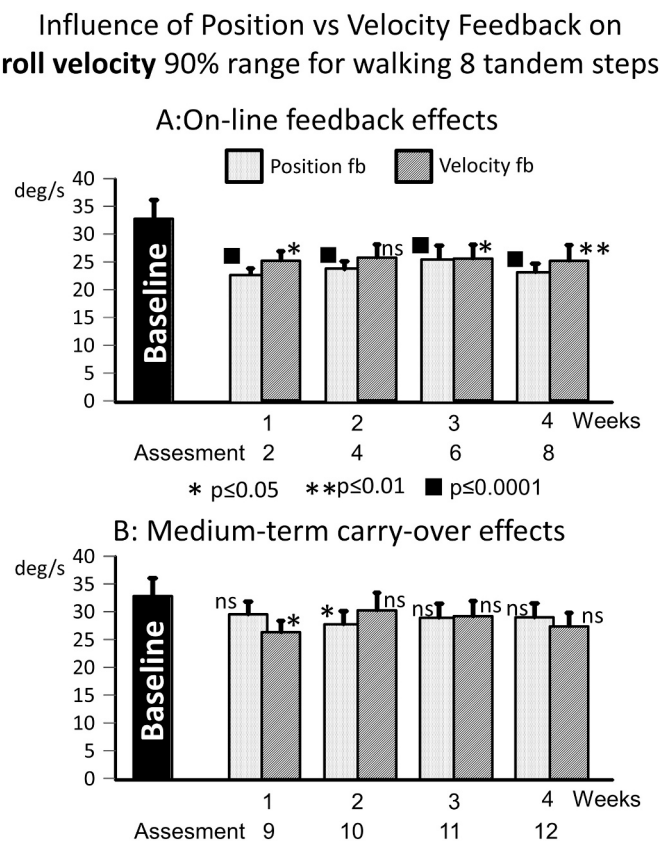

Fig. 5. Mean population sample values of the 90% range of trunk roll sway angular velocity for the task of walking 8 tandem steps with either angle or angular velocity feedback. A: On-line feedback effects for assessments 2, 4, 6, and 8 for which either position or velocity feedback was provided. B Medium-term carry-over effects observed in assessments 9, 10, 11 and 12 in the 4 weeks subsequent to feedback training. Details of the figure are provided in the legend to Fig. 3.

example, for the task with most improvement, standing on 1 leg, roll angle had a correlation of 0.32 with the DHI score after 4 weeks of training. In the weeks post VTfb training, DHI scores increased again, but nonetheless still with a significant improvement at 4 weeks of follow-up (26%, assessment 12) and at 6 months, assessment 13 (29%) (Fig. 7B and Table 5) with respect to baseline (assessment 1).

4. Discussion

This study explored the characteristics of the improvement in balance control when MS patients were provided sensory augmentation in the form of vibrotactile feedback (VTfb) of trunk sway. Apart from providing interesting scientific information on the effect of sensory augmentation on balance control for MS patients, the knowledge gained on these characteristics is crucial for clinical planning of rehabilitation strategies based on VTfb. Examining the direct feedback effects of VTfb, there was little difference in the changes in global balance scores when 1, 2, 3 or 4 weeks of training were provided (Fig. 3A). However, the short-term carry-over effect reached its best improvement at 4 weeks (Fig. 2B). Furthermore, a similar best improvement was reached in patients' DHI scores at 3 weeks (Fig. 7A). It would seem important to include this subjective rating of perceived balance capabilities when considering the length of a sensory augmentation training period. Most studies using VTfb have chosen to use training durations of 6 weeks similar to those of vestibular rehabilitation therapy [25,41,42] without consideration of possible criteria for selection of the optimal training duration. A rapid early improvement followed by a slower learning phase as we observed is typical of motor skill learning [43]. Based on the best improvement in short-term carry-over effects in balance and DHI scores, we would recommend using 3 weeks of VTfb training twice per week.

One important outcome of this study is the dominance of improvement in roll angle values both during training and after completion of the training (Table 3). Moreover, the tasks, which showed most improvement, were those likely to be most affected by roll instability: standing on one leg, walking over low barriers, walking tandem steps and tandem stance (Table 3). That is, the improvement was present for gait tasks with extended single stance phases. This finding supports previous work that patients with MS frequently present a lower-leg asymmetry in the form of muscle weakness or sensory loss [44,45], which results in lateral instability when tested with dynamic posturography (Tang, Allum, Yaldizli et al., unpublished observations). In other patient groups with asymmetrical disease effects (e.g. those with Parkinson's disease) roll angle and pitch velocity also showed the most improvement with VTfb training [46]. All these findings suggest that a simplification of the VTfb procedure providing only roll feedback might be worthwhile considering. When this was attempted with young healthy subjects, the reductions in stance and gait roll angles were greater with roll only versus pitch only VTfb [47]. Specifically, for the task of standing on one leg task the reduction in roll sway was greater for roll sway only VTfb than the reduction in pitch sway for pitch only VTfb.

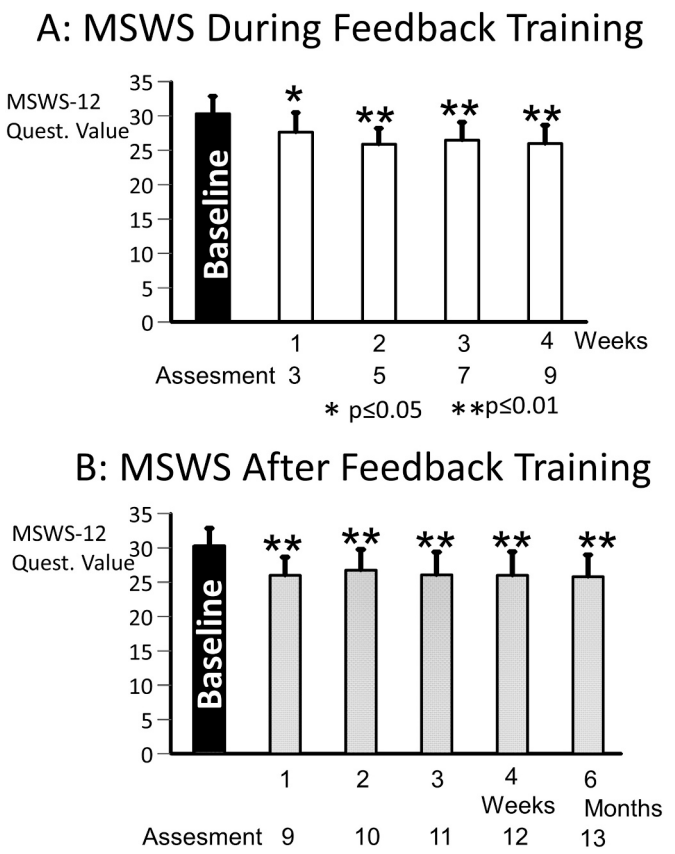

Fig. 6. Changes in the MSWS-12 questionnaire values during (A) and after (B) feedback training. The height of the column represents the mean value and the vertical bar on the column, the standard error of the mean. The significance (prior to Bonferroni corrections) of the difference of the means with respect to assessment 1 values (baseline) is indicated by asterisks on the columns. For the mean comparison to remain significant after Bonferroni correction p needed to be ≤0.01. There were no regression significant trends observed in mean MSWS values over weeks 1 to 4 during and after feedback training. Quest. stands for questionnaire.

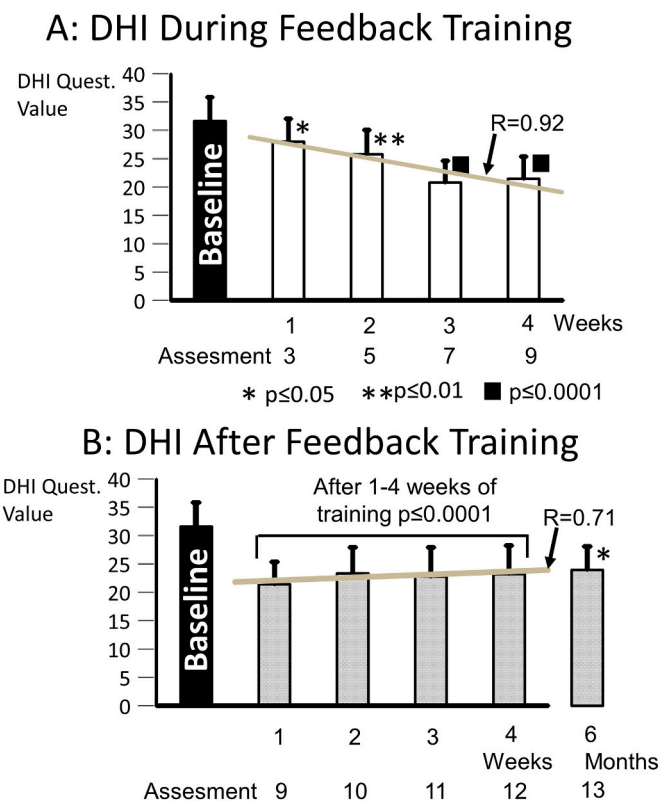

Fig. 7. Changes in DHI questionnaire values during (A) and after (B) feedback training. The height of the column represents the mean value and the vertical bar on the column, the standard error of the mean. The significance, prior to Bonferroni corrections) of the difference of the means with respect to assessment 1 values (baseline) is indicated by symbols above the columns in A, and by text in B. For the mean comparison to remain significant after Bonferroni correction p needed to be ≤0.01. There were significant trends in the regressions observed in MSWS values over weeks 1 to 4 during (R = 92, decreasing values over time) and after (R = 0.71, increasing values) feedback training.

Thus, further studies should explore the efficacy of providing only roll feedback in comparison to the multi-directional roll and pitch feedback (8 directions) used in this study.

The question of the duration of the carry-over effect once training had stopped is linked to the question whether to rely solely on the feedback effect and not on the carryover effect for improving balance in MS patients. That is, in the former case, the patient would be assumed to wear the device continuously. Although a carry-over effect was seen up to 2 months post training, the effect was not as strong as the feedback effect (see Tables 3 and 4). Our carry-over effect is less pronounced than that observed by Bao et al. [42] in their pilot study on vestibular loss patients, and more pronounced than that observed in other pilot studies on the elderly and patients with uncompensated unilateral vestibular loss [16]. In the study of Bao et al. [42] patients received a more intense and longer training protocol – 3 sessions a week for 8 weeks – which may have influenced the carry-over effect. In another study of carry-over effects, Brugnera et al. [48] showed a more significant improvement in the medium term carry-over effect for condition 6 (eyes closed on a sway-referenced platform) of the Equitest system which is an easier but comparable to the task standing eyes closed on foam task used in the current study [49]. However, there are also a number of differences between these studies, 10 vs 8 days of training, 6 vs 11 trained tasks respectively for the current study which could have influenced the results too. Nonetheless it may concluded from these studies that if patients did not choose to use the VTfb continuously, an alternative option

Table 5
Statistical descriptives for MSWS and DHI questionnaires at baseline (assessment 1), 1 week after training ceased (assessment 9), and 6 months after VTfb training ceased (assessment 13). DHI stands for Dizziness Handicap Inventory score; MSWS-12 for MS, 12 question, walking score.

MSWS-12	Baseline	1 week after training ceased	6 months after training ceased
	Assessment 1	Assessment 9	Assessment 13
Mean	30.3	26.0	24.8
Median	29.0	25.0	20.0
sem	2.6	2.6	3.0
sd	10.2	10.2	10.1
Min	15	14	12
Max	46	43	43
Range	31	29	31
DHI	Baseline	1 week after training ceased	6 months after training ceased
	Assessment 1	Assessment 9	Assessment 13
Mean	31.6	21.5	22.4
median	28.0	16.0	28.0
sem	4.2	3.9	4.1
sd	16.9	15.2	13.6
Min	8	2	6
Max	64	52	46
Range	58	50	40

would be to train them for 3 weeks and them to return for further training 2 months after training had stopped and the carry-over effects have "worn-off". Improving the latter option should be explored in future research. Improving the carry-over effect is a highly relevant aspect for those patients preferring not to wear a feedback device continuously.

A further interesting question is whether trunk angular or angular velocity feedback should drive the VTfb. Most of the previous studies which focussed on this question have suggested that a combination of the two would be optimal for control of stance, as above 0.5 Hz there is, based on modelling procedures, an increase of sway with solely angular position feedback [21,50]. Unfortunately, a theoretical framework examining this question for gait is missing. In our study we chose to use position feedback for stance trials and velocity feedback for gait trials based on previous work with chronic unilateral vestibular loss patients [51]. As recommended by Loughlin et al. [21] we set the position and velocity thresholds individually. We attempted to determine the more optimal mode of feedback was by using both position and velocity driven VTfb for tandem gait trials. Tandem gait can be considered a combined stance and gait task. Our results indicated that both modes of feedback were equally effective in reducing trunk sway when VTfb was present (Figs. 3 and 4, Table 4). However, carry-over effects for pitch were slightly greater for velocity VTfb. As we only tested one gait task, tandem steps, for differences between position and velocity driven VTfb, future studies should determine if combining the 2 modes of feedback as others have done [42,50] leads to improved effects for all gait tasks, further if the combination is disease specific. For example, MS patients may require a different feedback combination of position and velocity feedback from that of vestibular loss patients due to the former patient group having a proprioceptive loss.

We mounted the VTfb system within a head band. The feedback signal during gait was the pitch and roll angular velocity of the lower trunk (lumbar 1–3) roughly equivalent to the movement of the centre of mass. While such a system has the advantage of providing a rapid feedback to the CNS, being on the head, it has the disadvantage that the subject has to correct for the yaw rotation of the head movement when using the VTfb to drive balance control signals in the pitch and roll planes. A similar transformation must be employed when the CNS uses vestibular signals to drive balance control of the body's centre of mass. In fact, when subjects were asked to walk over low barriers, a task that involves large yaw (twisting about the body's longitudinal axis) rotations, the improvements were much greater for this task than when yaw rotations were less as during walking 8 m (Table 4), indicating that MS patients were able to perform the necessary spatial transformation of VTfb signals. Interestingly, the body's yaw rotations have not been coded into VTfb devices to date. Thus, it remains an open question whether this additional information would further improve balance control for MS patients.

The current study has a number of limitations. We are aware that MS patients can have a variety of neurological deficits (see Table1). Thus finding MS patients showing the same neurological deficits is difficult, as each case seems to have its own individual course. Nonetheless, there is a common pattern of neurological deficits affecting most MS patients, constituting of variable degrees of spastic paraparesis as was present in the majority of our patients. Secondly, our control cross-over study comparing the effects of VTfb with that of training the same tasks without VTfb had fewer subjects, 10, compared to 16 in the current study. It is possible that similar trends in balance improvements for the two studies would not have been observed with 16 subjects in the control study. Furthermore, 2 gait tasks (walking with head pitching with velocity VTfb and walking 8 tandem steps with position VTfb) did not feature in the control study which was designed to act as a control study for the current study as well as a control for other planned studies. Thus future RCT studies should take these factors into account. We were not able to demonstrate significant correlations between trunk sway measures and DHI scores, even for the variables and tasks (roll angle during standing on 1 leg or during tandem gait) at the time point of 3 weeks of training when we noted the most improvement with VTfb. Previous studies [33] had noted a correlation for MS subjects not receiving VTfb, however, for a greater number of subjects, a total of 37, and a greater range of EDSS scores (1.0 to 4.5) compared to the range of this study (2.5 to 4.0). Thus future studies should consider increasing the range of EDSS scores. Also, we did not collate information on the balance-oriented physiotherapy received by the patients prior to and during the current study which might have influenced our results.

Another limitation of the current study is longer duration of training we compared to that of our control study [22]. We designed the current study to determine short-term and medium-term effects of VTfb training, and noted that the initial (1st week) short-term feed-back effects were significantly greater than control training effects determined in our previous cross-over study [22]. Thus the question arises whether our control study should have had a longer period of training under the assumption that a longer period of training might have brought greater improvements equaling those obtained with VTfb. In the current study, we found a rapid initial short-term feedback-effect as in our previous studies [22] accompanied by a slow improvement in the short-term (first 4 weeks) feedback and carry-over effects and followed by slow reduction of the medium-term (second 4 weeks) carry-over effect post training. If the short-term carry-over effects were equally effective for training of a control group without VT feedback, then we should have seen that the carry-over effects during the first 4 weeks of training were stronger than the effect of feedback because, presumably, these effects (carry-over from feedback training and training due to the assessments without feedback) would then have been additive effects. We saw no evidence for this in the short-term carry-over effects but it should be noted that separating these additive effects is complicated. A control group receiving no VTfb, only training for a period of 4 weeks might have brought more information on the magnitude of training and VTfb carry-over effects compared to a control group. Another question that arises is if the short-term carry-over effect would have been larger if we had tested for this immediately after the VTfb assessments rather than 3 days later. We chose this procedure for 2 reasons. Firstly, we wanted to avoid fatiguing the MS patients, and secondly our primary interest was in the medium and long-term carry-over effects in order to determine when patients should return for further training once these later effects have "worn-off".

In this study we specifically excluded some difficult tasks such as walking up and down a set of stairs without handrails as we had noted in previous studies [34] that these tests were too difficult for most MS patients with EDSS scores of 3 and higher to perform. It is an open question whether the approach taken by Bao et al. [42] to adapt the exercise regime to the patient's balance abilities, providing more challenging exercises for those with superior balance control, would have led to different results to those described in the current study.

In conclusion, a 3 week VTfb training program demonstrated the most significant improvement in the short term carry-over effect on the balance control of MS patients. An additional week of training did not result in further improvements to balance control. Similar results were obtained from the patients' subjectively assessed balance capabilities (PROMs). The carry over effects of VTfb on balance control lasted 2 months. At this time, patients would need to receive further training if not using the VTfb system continuously. We found most improvement both in terms of body sway angles and durations for stance and gait tasks involving 1-legged stance phases. A practical example is walking over low barriers. We found no difference between using velocity or position VTfb for the limited number of tasks we explored. Patients seemed capable of adapting to both types of feedback.

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Declaration of Competing Interest

JHJ Allum worked as a consultant for the company "Balance International Innovations GmbH" which manufactured the SwayStar™ posturography system used in this study. Ö Yaldizli, V Haller, T Derfuss, and J Kuhle received consultancy and travel fees from several pharmaceutical companies including: Allmirall, Biogen, Merck, Novartis, Roche, and Sanofi Genzyme among others.

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References

[1] J. Correale, M.I. Gaitán, M.C. Ysrraelit, M.P. Fiol, Progressive multiple sclerosis: from pathogenic mechanisms to treatment, Brain 140 (2016) 527–546.
[2] J. Oh, A. Vidal Jordana, X. Montalban, Multiple sclerosis: clinical aspects, Curr. Opin. Neurol. 31 (2018) 752–759.
[3] P. Browne, D. Chandraratna, C. Angood, H. Tremlett, C. Baker, B. Taylor, et al., Atlas of multiple sclerosis 2013: a growing global problem with widespread inequity, Neurology 83 (2014) 1022–1024.
[4] E. Blozik, R. Rapold, K. Eichler, O. Reich, Epidemiology and costs of multiple sclerosis in Switzerland: an analysis of health-care claims data, 2011-2015, Neuropsychiatr. Dis. Treat. 13 (2017) 2737–2745.
[5] M. Kaufmann, M.A. Puhan, J. Kuhle, Ö. Yaldizli, T. Magnusson, C.P. Kamm, et al., A framework for estimating the burden of chronic diseases: design and application in the context of multiple sclerosis, Front. Neurol. 10 (2019) 953.
[6] L. Comber, J.J. Sosnoff, R. Galvin, S. Coote, Postural control deficits in people with multiple sclerosis: a systematic review and meta-analysis, Gait Posture 61 (2018) 445–452.
[7] O. Kantarci, B. Weinshenker, Natural history of multiple sclerosis, Neurol. Clin. 23 (2005) 17–38.
[8] F. Bethoux, Gait disorders in multiple sclerosis, Continuum (Minneap Minn) 19 (2013) 1007–1022.
[9] M.H. Cameron, F.B. Horak, R.R. Herndon, D. Bourdette, Imbalance in multiple sclerosis: a result of slowed spinal somatosensory conduction, Somatosens. Mot. Res. 25 (2008) 113–122.
[10] R.H.B. Benedict, R. Holtzer, R. Motl, F. Foley, S. Kaur, D. Hojnacki, et al., Upper and lower extremity motor function and cognitive impairment in multiple sclerosis, J. Int. Neuropsychol. Soc. 17 (2011) 643–653.
[11] R. Doty, M. MacGillivray, H. Talab, I. Tourbier, M. Reish, S. Davis, et al., Balance in multiple sclerosis: relationship to central brain regions, Exp. Brain Res. 236 (2018) 2739–2750.
[12] M.H. Cameron, S. Lord, Postural control in multiple sclerosis: implications for fall prevention, Curr. Neurol. Neurosci. Rep. 10 (2010) 407–412.
[13] K.M.T. Goutier, S.L. Jansen, C.G.C. Horlings, U.M. Küng, J.H.J. Allum, The influence of walking speed and gender on trunk sway for the healthy young and older adults, Age Ageing 39 (2010) 647–650.
[14] M. Hulliger, N. Dürmüller, A. Prochazka, P. Trend, Flexible fusimotor control of muscle spindle feedback during a variety of natural movements, Prog. Brain Res. 80 (1989) 87–101 (discussion 57-60).
[15] K.H. Sienko, M.D. Balkwill, L.I.E. Oddsson, C. Wall, Effects of multi-directional vibrotactile feedback on vestibular-deficient postural performance during continuous multi-directional support surface perturbations, J. Vestib. Res. 18 (2008) 273–285.
[16] J.H.J. Allum, M.G. Carpenter, B.C. Horslen, J.R. Davis, F. Honegger, K.S. Tang, et al., Improving impaired balance function: Real-time versus carry-over effects of prosthetic feedback, in: Conf Proc IEEE Eng Med Biol Soc; 2011 Aug. 30 2011-Sept. 3 2011, 2011.
[17] K. Bark, J. Wheeler, P. Shull, J. Savall, M. Cutkosky, Rotational skin stretch feedback: a wearable haptic display for motion, IEEE Trans. Haptics 3 (2010) 166–176.
[18] C. Wall, M.S. Weinberg, P.B. Schmidt, D.E. Krebs, Balance prosthesis based on micromechanical sensors using vibrotactile feedback of tilt, IEEE Trans. Biomed. Eng. 48 (2001) 1153–1161.
[19] J.R. Davis, M.G. Carpenter, R. Tschanz, S. Meyes, D. Debrunner, J. Burger, et al., Trunk sway reductions in young and older adults using multi-modal biofeedback, Gait Posture 31 (2010) 465–472.
[20] F. Honegger, I.M.A. Hillebrandt, N.G.A. van den Elzen, K.-S. Tang, J.H.J. Allum, The effect of prosthetic feedback on the strategies and synergies used by vestibular loss subjects to control stance, J. Neuroeng. Rehabil. 10 (2013) 115.
[21] P. Loughlin, A. Mahboobin, J. Furman, Designing vibrotactile balance feedback for desired body sway reductions, in: Conf Proc IEEE Eng Med Biol Soc; 2011 Aug. 30 2011-Sept. 3 2011, 2011.
[22] R.P. van der Logt, O. Findling, H. Rust, O. Yaldizli, J.H.J. Allum, The effect of vibrotactile biofeedback of trunk sway on balance control in multiple sclerosis, Mult. Scler. Rel. Dis. 8 (2016) 58–63.
[23] L.L. Verhoeff, C.G.C. Horlings, L.J.F. Janssen, S.A. Bridenbaugh, J.H.J. Allum, Effects of biofeedback on trunk sway during dual tasking in the healthy young and elderly, Gait Posture 30 (2009) 76–81.
[24] L. Prosperini, L. Castelli, F. De Luca, F. Fabiano, I. Ferrante, L. De Giglio, Task-dependent deterioration of balance underpinning cognitive-postural interference in MS, Neurology 87 (2016) 1085–1092.
[25] C.Z.-H. Ma, D.W.-C. Wong, W.K. Lam, A.H.-P. Wan, W.C.-C. Lee, Balance improvement effects of biofeedback systems with state-of-the-art wearable sensors: a systematic review, Sensors 16 (2016) 434.
[26] H.M. Rust, N. Lutz, V. Zumbrunnen, M. Imhof, Ö. Yaldizli, V. Haller, et al., Benefits of short-term training with vibrotactile biofeedback of trunk sway on balance control in multiple sclerosis, Phys. Med. Rehabil. Res. 5 (2020) 1–10.
[27] C. Polman, S. Reingold, B. Banwell, M. Clanet, J. Cohen, M. Filippi, et al., Diagnostic criteria for multiple sclerosis: 2010 revisions to the McDonald criteria, Ann. Neurol. 69 (2011) 292–302.
[28] G.P. Jacobson, C.W. Newman, The development of the dizziness handicap inventory, Arch. Otolaryngol. Head Neck Surg. 116 (1990) 424–427.
[29] J.C. Hobart, A. Riazi, D.L. Lamping, R. Fitzpatrick, A.J. Thompson, Measuring the impact of MS on walking ability: the 12-item MS walking scale (MSWS-12), Neurology 60 (2003) 31–36.
[30] D. Cattaneo, A. Regola, M. Meotti, Validity of six balance disorders scales in persons with multiple sclerosis, Disabil. Rehabil. 28 (2006) 789–795.
[31] M.E. Tinetti, Performance-oriented assessment of mobility problems in elderly patients, J. Am. Geriatr. Soc. 34 (1986) 119–126.
[32] A. Shumway-Cook, F.B. Horak, Assessing the influence of sensory interaction of balance. Suggestion from the field, Phys. Ther. 66 (1986) 1548–1550.
[33] S.H. Corporaal, H. Gensicke, J. Kuhle, L. Kappos, J.H. Allum, O. Yaldizli, Balance control in multiple sclerosis: correlations of trunk sway during stance and gait tests with disease severity, Gait Posture 37 (2013) 55–60.
[34] M.H. Fanchamps, H. Gensicke, J. Kuhle, L. Kappos, J.H. Allum, O. Yaldizli, Screening for balance disorders in mildly affected multiple sclerosis patients, J. Neurol. 259 (2012) 1413–1419.
[35] A. Sehle, A. Mündermann, K. Starrost, S. Sailer, I. Becher, C. Dettmers, et al., Objective assessment of motor fatigue in multiple sclerosis using kinematic gait analysis: a pilot study, J. Neuroeng. Rehabil. 8 (2011) 59.
[36] J. Hegeman, E.Y. Shapkova, F. Honegger, J.H.J. Allum, Effect of age and height on trunk sway during stance and gait, J. Vestib. Res. 17 (2007) 75–87.
[37] J.H. Allum, A.L. Adkin, Improvements in trunk sway observed for stance and gait tasks during recovery from an acute unilateral peripheral vestibular deficit, Audiol. Neurootol. 8 (2003) 286–302.
[38] A. Galecki, T. Burzykowski, Linear Mixed-Effects Models Using R. A Step-by-Step Approach, Springer-Verlag, New York, 2013.
[39] R Core Team, R: A Language and Environment for Statistical Computing [Internet], R Foundation for Statistical Computing, 2020. Available from: https://www.R-project.org/.
[40] J. Pinheiro, D. Bates, S. DebRoy, D. Sarkar, R. Core Team, nlme: Linear and Nonlinear Mixed Effects Models, R package version 3.1-152, https://CRAN.R-project.org/package=nlme, 2021.
[41] D. Basta, M. Rossi-Izquierdo, A. Soto-Varela, M.E. Greters, R.S. Bittar, E. Steinhagen-Thiessen, et al., Efficacy of a vibrotactile neurofeedback training in stance and gait conditions for the treatment of balance deficits: a double-blind, placebo-controlled multicenter study, Otol. Neurotol. 32 (2011) 1492–1499.
[42] T. Bao, B.N. Klatt, W.J. Carender, C. Kinnaird, S. Alsubaie, S.L. Whitney, et al., Effects of long-term vestibular rehabilitation therapy with vibrotactile sensory augmentation for people with unilateral vestibular disorders – A randomized preliminary study, J. Vestib. Res. 29 (2019) 323–334.
[43] E. Dayan, L. Cohen, Neuroplasticity subserving motor skill learning, Neuron 72 (2011) 443–454.
[44] T.F. Scott, K. Bhagavatula, P.J. Snyder, C. Chieffe, Transverse myelitis. Comparison with spinal cord presentations of multiple sclerosis, Neurology 50 (1998) 429–433.
[45] T. Rudroff, F. Proessl, Effects of muscle function and limb loading asymmetries on gait and balance in people with multiple sclerosis, Front. Physiol. 9 (2018) 531.
[46] W. Nanhoe-Mahabier, J.H. Allum, E.P. Pasman, S. Overeem, B.R. Bloem, The effects of vibrotactile biofeedback training on trunk sway in Parkinson's disease patients, Parkinsonism Relat. Disord. 18 (2012) 1017–1021.
[47] L.J. Janssen, L.L. Verhoeff, C.G. Horlings, J.H. Allum, Directional effects of biofeedback on trunk sway during gait tasks in healthy young subjects, Gait Posture 29 (2009) 575–581.
[48] C. Brugnera, R.S.M. Bittar, M. Greters, D. Basta, Effects of vibrotactile vestibular substitution on vestibular rehabilitation – Preliminary study, Braz. J. Otorhinolaryngol. 81 (2015) 616–621.
[49] J.H.J. Allum, F. Zamani, A.L. Adkin, A. Ernst, Differences between trunk sway characteristics on a foam support surface and on the Equitest® ankle-sway-referenced support surface, Gait Posture 16 (2002) 264–270.
[50] A.D. Goodworth, I.C. Wall, R.J. Peterka, Influence of feedback parameters on performance of a Vibrotactile balance prosthesis, IEEE Trans. Neural. Syst. Rehabil. Eng. 17 (2009) 397–408.
[51] J. Hegeman, F. Honegger, M. Kupper, J.H.J. Allum, The balance control of bilateral peripheral vestibular loss subjects and its improvement with auditory prosthetic feedback, J. Vestib. Res. 15 (2005) 109–117.